REMARKS

Favorable reconsideration is respectfully requested in view of following remarks.

Claims 12, 13 and 15-23 are pending.

Claims 12, 13, 15, 16 and 23 were examined on the merits and stand rejected.

Claims 17-22 are withdrawn.

On pages 3-8 of the Office Action, claims 12-13, 15-16 and 23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Zarling et al. (US 2004/0019916) in view of Moriya (Proc. Natl. Acad. Sci. USA, Vol. 90 pp. 1122-1126).

Applicants respectfully traverse this rejection.

The Examiner alleges that:

(1) Zarling et al. teaches an in vitro base conversion method of a cDNA sequence, which is a method of converting one or more bases in a target DNA sequence in a cell, but Zarling et al. does not teach preparing a single-stranded DNA fragment by cleavage from a single-stranded circular DNA;

(2) Moriya teaches use of shuttle phagemid vectors for production of single stranded DNA. One of ordinary skill in the art knows that shuttle phagemid vectors have architecture that allows one to express the desired (+ sense strand) or (- antisense strand) strand. So 100% of the DNA produced as single stranded DNA can be the desired sense or antisense strand.

(3) If one desires to have 100% population containing only either the + or - strand, then the target gene of appropriate fragment size can be cloned in the multiple cloning site of the chosen phagemid vector.

Applicants respectfully question the Examiner's assertion above in part (3). The Examiner has not provided motivation to produce a population containing either only the + or - strand for base conversion method. Zarling et al. describes that a mixture of + and - strands prepared from PCR products can be effective for base conversion of a target gene. How would one of skill in the art know that only the + or - strand would be more effective?

The concept of the claimed invention is that use of the single-stranded ***sense*** DNA enhances the efficiency of base conversion of a target gene in a cell. This inventive concept is not disclosed or suggested in Zarling et al. There is no motivation for one of in the art of base conversion to produce only + or - strand DNA fragment from phagemid vector.

Applicants furthermore refer to MPEP 2142:

> The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also *KSR,* 550 U.S. at ___ , 82 USPQ2d at 1396 (quoting Federal Circuit statement with approval).

Applicants respectfully suggest that the Examiner has merely shown that plus or minus strains can be made but has not articulated reasoning with some rational underpinning to support combination of single strain sense DNA fragment with the teachings of Zarling.

The Examiner also rejects the applicants' arguments as to superior conversion efficiency of the invention, because the instant claims do not recite any particular conditions that affect efficiency of conversion. However, Applicants note that use of a sense-stranded DNA fragment inherently has superior efficiency compared with other DNA fragment(s). Examples in the present application compare base conversion efficiencies of the following DNA fragments under the same conditions:

(a) single-stranded sense DNA fragment (the present invention);

(b) single-stranded antisense DNA fragment;

(c) mixture of sense and antisense DNA fragments that are prepared by denaturation of a double-stranded DNA fragment; and

(d) mixture of sense and antisense DNA fragments that are prepared by denaturation of a PCR product (Zarling et al.).

The examples in the specification show the superior efficiency of single-stranded sense DNA fragment, which does not depend on other conditions. For instance, please see Figs. 3 and 4.

Thus, Applicants respectfully request the Examiner to again consider the evidence of superior conversion efficiency shown in the specification. Such superior conversion efficiency is due to use of single-stranded sense DNA fragment and therefore is recited in the claims. It is superfluous to further indicate in the claims that there is superior conversion efficiency as such is an inherent effect of using single-stranded sense DNA. Furthermore, although the Examiner is

correct that absolute conversion efficiency is affected by numerous variables, the use of single-stranded sense DNA will always result in superior conversion efficiency when compared to other DNA mixtures under the same conditions. The Examiner's contention that manipulation of other variables will result in conversion efficiencies variations may be correct but seems to be illogical. To indicate that the claimed invention does not enhance conversion efficiency by comparison of reactions with different DNA mixtures (single or double stranded) and different reaction conditions is not a true comparison. A person of skill in the art clearly understands that enhance conversion efficiency of the claimed invention refers to comparison of two identical reactions except for the DNA mixture.

Thus, Applicants note that (1) the Examiner has failed to provide an articulated reason for combining the references and (2) the Examiner has failed to consider that the use of single-stranded sense DNA enhances efficiency of base conversion. Thus, for the above-noted reasons, Applicants respectfully contend that this rejection is untenable and should be withdrawn.

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Hiroyuki KAMIYA et al.

/William R. Schmidt, II/

Digitally signed by /William R. Schmidt, II/
DN: cn=/William R. Schmidt, II/, o, ou, email=bschmidt@wenderoth.com, c=US
Date: 2011.05.13 15:25:46 -04'00'

By _____
William R. Schmidt, II
Registration No. 58,327
Attorney for Applicants

WRS/vah
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
May 13, 2011